UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,653	11/16/2006	Wei Cheng	05-937-B5	5425

20306 7590 02/03/2010

MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER	
JAISLE, CECILIA M	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
02/03/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/576,653	**Applicant(s)** CHENG ET AL.	
	Examiner Cecilia M. Jaisle	**Art Unit** 1624	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 January 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *13-29,34 and 35*.
   Claim(s) objected to: _____.
   Claim(s) rejected: *40*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624

/Cecilia M. Jaisle/
Examiner, Art Unit 1624

Continuation of 3. NOTE: Proposed amended claim 40 would be rejectable under 35 USC 112, paragraph 1, as failing to comply with the enablement requirement. Claim 40 recites treating cancer, rheumatoid arthritis, graft-host diseases, multiple sclerosiie, psoriasis, artheroscrosis [sic]. myocardioinfarction [sic[, ischemis, stroke, diabetes, obesity, hypercholesterolemis, interbowel [sic[diseases, osteoarthritus [sic], macular degeneration and diabetic retinopathy.

The specification asserts the claimed compounds inhibit, regulate or modulate kinase or p70S6K activity and are therefor of value in the above recited conditions, for which insufficient enablement is provided.

Substantiation of utility and its scope is required when utility is "speculative," "sufficiently unusual" or not provided. See Ex parte Jovanovics, et al., 211 USPQ 907, 909 (BPAI 1981). Hoffman v. Klaus, 9 USPQ2d 1657 (BPAI 1988) and Ex parte Powers, 220 USPQ 924 (BPAI 1982) regarding types of testing needed to support in vivo uses.

Applicants' attention is drawn to the Revised Interim Utility and Written Description Guidelines, 66 FR 1092-1099 (2001), emphasizing "a claimed invention must have a specific and substantial utility." MPEP 2163, et. seq. This disclosure is insufficient to enable the claimed methods based on the disclosed PDE2 inhibition.

MPEP § 2164.01(a) states:

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Many factors require consideration when determining whether sufficient evidence supports a conclusion that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue." MPEP 2164.01(a). These factors include: (1) the claim breadth; (2) the nature of the invention; (3) the state of the prior art; (4) the level of predictability in the art; (5) the amount of direction provided by the inventor; (6) the presence of working examples; and (7) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)(reversing the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement). See also In re Goodman 29 USPQ2d 2010, 2013 (Fed. Cir. 1993). Application of these factors to the present application supports the determination that the present disclosure fails to satisfy the enablement requirement:

1. Breadth of the claim:

(a) Scope of the methods. The claim covers methods using substituted pyrimidine compounds.

(b) Scope of the conditions covered. The claims cover methods to treat above conditions.

Modulate p70S6K activity in vivo. p70 ribosomal protein S6 kinase (p70S6K) participates in protein synthesis control and activates in response to hormones, mitogens and nutrients. p70S6K phosphorylates the 40S ribosomal protein S6, which is involved in translation of certain mRNAs, the 5'-TOP mRNAs encoding ribosomal proteins and elongation factors. p70S6K is activated by insulin in muscle, but not in hepatocytes. In these cells, p70S6K is activated by amino acids like glutamine and leucine, which act synergistically. However, crosstalk between insulin and amino acids can be demonstrated with leucine, which enhances insulin signaling towards p70S6K in many cell types, including hepatocytes.

The mechanism of p70S6K activation involves a complex sequence of multiple serine/threonine phosphorylations catalyzed by several protein kinases. One of these is the mammalian target of rapamycin (mTOR), which phosphorylates p70S6K on Thr389 and is inhibited by the immunosuppressant rapamycin. Phosphorylation of this site correlates with kinase activity. mTOR may also phosphorylate and thereby inactivate a protein phosphatase that in turn inactivates p70S6K. The amino-acid signaling pathway leading to p70S6K activation may comprise inhibition of protein phosphatase. Whatever the activation mechanism of p70S6K by mTOR, the latter plays an essential role, because p70S6K activation caused by almost all stimuli is inhibited by rapamycin. Phosphorylation of Ser411, Thr421 and Ser424, which are within a Ser-Pro rich region located in the autoinhibitory domain, is also thought to modulate p70S6K activity. In response to insulin, 3-phosphoinositide-dependent protein kinase (PDK1) is directly involved in p70S6K activation. Target phosphorylation site for PDK1 is Thr229 in the p70S6K catalytic domain.

Acetyl-CoA carboxylase (ACC) is a regulatory enzyme in fatty acid synthesis. In liver cells ACC activation is correlated with cell swelling induced by amino acids cotransported with Na+ or by hypotonic medium. ACC activity is controlled by various mechanisms, including changes in the degree of polymerization, allosteric regulation by citrate and glutamate and covalent modification by phosphorylation/dephosphor-ylation. The active form is generally assumed to be dephosphorylated, although phosphorylation has been invoked to explain ACC activation by insulin in adipocytes.

Under stress conditions, such as anoxia or inhibition of mitochondrial oxidative phosphorylation, ATP balance becomes negative and the AMP/ATP ratio increases. This leads to AMP-activated protein kinase (AMPK) activation, which functions as a metabolic master switch and inhibits anabolic processes, preserving ATP. ACC is phosphorylated in vitro by AMPK on Ser79, Ser1200 and Ser1250, the phosphorylation of Ser79 being responsible for inactivation. AMPK-inactivated ACC can be reactivated by a glutamate-dependent type-2A protein phosphatase (GAPP), which dephosphorylates a synthetic peptide encompassing the Ser79 phosphorylation site for AMPK in ACC. In hepatocytes the activation ACC state is expected to result from balance between GAPP and AMPK activities, although involvement of other protein kinase or phosphatases has not been ruled out.

Because ACC and p70S6K display a similar and parallel pattern of activation in hepatocytes incubated with glutamine, the question arises whether there is also a common mechanism for inactivation. It is indeed expected that ACC and p70S6K, which control energy-consuming biosynthetic pathways, are less active when ATP supply becomes limiting. The effect of different AMPK activators and the effect of protein phosphatase inhibitors the amino-acid-induced ACC and p70S6K activation were examined in freshly prepared rat hepatocytes. Results show that ACC and p70S6K activation depend on protein phosphatase and both enzymes may be inactivated under conditions leading to AMPK activation.

Kinases (phosphotransferase) are enzyme types that transfer phosphate groups from high-energy donor molecules, e.g., ATP, to specific target molecules (substrates); the process is termed phosphorylation. An enzyme that removes phosphate groups from targets is known as a phosphatase. One of the largest kinase groups are protein kinases, which act on and modify activity of specific proteins, transmit signals and control complex cell processes. Up to 518 different human kinases have been identified. Various other kinases act on small molecules (lipids, carbohydrates, amino acids, nucleotides, and more), either for signaling or to prime them for biochemical reactions in metabolism. Uncontrolled, abnormal or unwanted cellular activities. It is not possible to know what is intended by "diseases or disorders associated with uncontrolled, abnormal and/or unwanted cellular activities.

o "In polycythemia vera, uncontrolled and rapid cellular reproduction and maturation cause proliferation or hyperplasia of all

bone marrow cells. The cause of such uncontrolled cellular activity is probably due to a multipotential stemcell defect." Do the methods of this invention treat polycythemia vera?

o A genetic predisposition with inadequate immune responses and uncontrolled cellular activity may make some women more susceptible to cervical cancer. Do the methods of this invention treat cervical cancer?

o Dreams are caused mostly by uncontrolled cellular activity. Do the methods of this invention alleviate treat uncontrolled, abnormal and/or unwanted dreams?

o A benign tumor is any abnormal cellular growth that remains confined to one area, is not cancerous and does not spread to distant body areas. Do the methods of this invention treat benign tumors?

o Abnormal cellular activity is often one predisposing factor for human osteosarcoma. Do the methods of this invention treat osteosarcoma?

o Inflammation and gene expression can be considered unwanted cellular activities. Do these inventive methods treat inflammation and gene expression?

Inhibition of cell proliferative activity. Mild intracellular redox imbalance inhibits cell proliferation independent of reactive oxygen species generation. Inhibition of the growth of hepatocellular carcinoma has been attributed to a decrease of cell proliferative activity. Indole-3-carbinol selectively inhibits cell proliferative activity induced by estradiol in responsive human breast cancer cells and phosphorylation of the estrogen receptor. CD54 and CD106 are involved in the ability of follicular dendritic cells to inhibit T-cell proliferative responses. Conjugated linoleic acid may act by antioxidant mechanisms, prooxidant cytotoxicity, inhibition of nucleotide and protein synthesis, reduction of cell proliferative activity and inhibition of both DNA-adduct formation and carcinogen activation. In male Syrian hamsters, stress influences epidermal cell proliferative activity and sebaceous gland activity.

Inhibition of abnormal cell metabolic activity. Increasing oxygen delivery to the myocardium so that the mitochondria can make more ATP via aerobic mechanisms and/or by decreasing heart rate and arterial blood pressure and thus, the rate of ATP breakdown by tissue, are pharmacologic therapies aimed at reducing abnormal cell metabolism to treat chronic stable angina.

The specification fails to identify treatment results with methods of this invention and how to recognize such results. Each of the above conditions has various symptoms and there is no indication of which specific symptoms are alleviated.

Cancer includes breast and colon cancers, carcinomas of the prostate, lymphoma, leukemia and many others. Breast cancers come in great variety. The most important category of breast cancers is the ductal cancers, which come in a wide variety of types, divided into categories: intraductal (in situ); invasive with pre-dominant intraductal component; invasive, NOS; comedo; inflammatory (IBC); medullary with lymphocytic infiltrate; mucinous (colloid) carcinoma; papillary carcin-oma; scirrhous; tubular and others. Another category is lobular breast cancers: in situ, invasive with predominant in situ component and invasive. Paget's disease of the nipple can be also with intraductal carcinoma or with invasive ductal carcinoma. Adenomyoepithelioma is a dimorphic tumor characterized by the presence of both epithelial and myoepithelial cells. There is breast angiolipoma and spindle cell lip-oma of the breast. There is lymphoma of the breast (which exists in both Non-Hodg-kin's lymphoma of the breast and Hodgkin's disease of breast forms). There are some sarcomas, including giant cell sarcoma of the breast, leiomyosarcoma of the breast, Angiosarcoma of the breast, cystosarcoma phylloides and liposarcoma of the breast. There are carcinoid tumors that can be primary carcinoid tumors of the breast or can arise from nonmammary sources. There are breast salivary gland-like tumors, including acinic cell carcinoma, oncocytic carcinoma (Mammary epithelial oncocytoma) and mucoepidermoid carcinoma. Other rare carcinomas include Spin-dle cell carcinoma of the breast, Squamous cell carcinoma of the breast, Secretory Carcinoma of the Breast (Juvenile secretory carcinoma), Metaplastic carcinoma of the breast (a heterogeneous group of invasive breast cancers including types with squamous differentiation and those with heterologous elements), Invasive Micropap-illary Carcinoma of the Breast, Adenoid cystic carcinoma of the breast, cribriform carcinoma, Myofibroblastoma of the Breast (Benign spindle stromal tumor of the breast) and glycogen-rich clear cell carcinoma of the breast. There are numerous other rare breast cancers, including for example Fibromatosis of the breast (extra-abdominal desmoid), Angiomatosis of the Breast and mammary hamartoma. There are also nonmammary tumors, primarily adenocarcinomas, that can metastasize to the breast, including bronchogenic carcinomas, malignant melanomas (primary and secondary), rhabdomyosarcomas, malignant mesotheliomas, thyroid carcinomas, renal cell carcinomas, malignant lymphomas and gastrointestinal carcinomas (including those from the stomach, pancreas, esophagus and colon).

The category of colon cancers includes many types which are rather diverse. Most are adenocarcinomas, either of the mucinous (colloid) type or the signet ring type. Less common colon cancers include squamous cell, neuroendocrine carcino-mas, carcinomas of the scirrhous type, lymphomas, melanomas (primary or meta-static), sarcomas (fibrosarcomas and Leiomyosarcomas) and Carcinoid tumors.

Carcinomas of the prostate are usually adenocarcinomas, but others include small cell carcinoma, mucinous carcinoma, prostatic ductal carcinoma, squamous cell carcinoma of the prostate, basal cell carcinoma, neuro-endocrine carcinoma, signet-ring cell carcinomas and others.

It is not understood what is meant by graft-host diseases, myocardioinfarction, interbowel diseases or osteoarthritus.

Diabetes includes Type-I diabetes, Type-II diabetes, diabetes insipidus, gestational diabetes, neurogenic diabetes, nephrogenic diabetes and dipsogenic diabetes. Each of these diseases requires different treatment.

2. Nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 166 USPQ 18, 24 (CCPA 1970).

Pharmacological activity in general is unpredictable. In applications involving physiological activity, such as the present:

The first paragraph of 35 U.S.C. §112 effectively requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.

Plant Genetic Systems v. DeKalb Genetics Corp., 65 USPQ2d 1452 (CAFC 2003).

3. Direction and Guidance: That provided is very limited. The dosage range information is meager at best. It is generic, the same for all disorders the specification covers. No specific direction or guidance provides a regimen or dosage effective specifically for all of the conditions construed by the claim.

4. State of the prior art: The art indicates the need for undue experimentation.

The anti-proliferative effects of sirolimus (Rapamycin, a p70S6K inhibitor) may have a role in treating cancer, but Rapamycin shows no effect on its own. Doxorubicin and sirolimus combination therapy has been shown to drive AKT-positive lymphomas into remission in mice. Bcl-2-positive lymphomas were completely resistant to sirolimus therapy; eIF4E expressing lymphomas are not sensitive to sirolimus. As with all immunosuppressive medications, Rapamycin decreases the body's inherent anti-cancer activity and allows some cancers to

proliferate, which would otherwise have been naturally destroyed. Wikipedia, Sirolimus (already of record).
Sawyers, Nature Reviews - Cancer (already of record), studying rapamycin use in renal cancer treatment, detected that rapamycin delivery to tumor cells is impaired in some patients and concluded, "This trial shows the importance of investigating drug delivery to tumour cells and target modulation in patients to guide future clinical development of targeted agents. Further study of rapamycin in PTEN-deficient glioblastoma is warranted."
Ability of any and all kinases or a p70S6K inhibitor to effectively treat all conditions encompassed by the claims remains open to further study and proof.
5. Working Examples: Applicants do not provide highly predictive competent evid-ence or recognized tests of all recited conditions the claims encompass. Applicants do not provide competent evidence that the instantly disclosed tests are highly predictive for all uses covered embraced by claim language for all intended hosts.
6. Skill of those in the art: Wikipedia and Sawyers call into question treatment with the claimed methods and confirm the need for additional research.
7. Quantity of experimentation needed to make or use the invention. Based on the disclosure's content, one skilled in the pharmaceutical arts would have an undue burden to use the invention, since the disclosure gives the skilled artisan inadequate guidance regarding pharmaceutical use, for reasons explained above. The state of the art, as discussed in the articles above, indicates the requirement for undue experimentation. The ability of an agent that treats all conditions construed by the claims remains open to further study and proof.
See MPEP 2164.01(a), discussed supra, justifying the conclusion of lack of enablement commensurate with the claim. Undue experimentation will be required to practice Applicants' invention.
Sitrick v. Dreamworks LLC, 85 USPQ2d 1826, 1830 (Fed. Cir. 2008) decided that a claim is not enabled when the claim covers multiple embodiments but the specification fails to enable all of the embodiments. "Because the asserted claims are broad enough to cover both [embodiments], the [specification] must enable both embodiments." Here, the claims at issue cover many embodiments and do not enable any of them.
Automotive Tech. Int'l. v. BMW of N. America, Inc., 84 USPQ2d 1108, 1116 (Fed. Cir. 2007) decided that a claim is not enabled when the claim covers multiple embodiments but the specification fails to enable one of the embodiments. "Thus, in order to fulfill the enablement requirement, the specification must enable the full scope of the claims that includes both [embodiments], which the specification fails to do." Here, the claims at issue cover many embodiments and do not enable any of them.

Proposed amended Claim 40 would also be rejected under 35 USC 112, paragraph 2, for failure to particular point out and distinctly claim the intended subject matter. The category of cancers includes many types which are rather diverse. It is not understood what is meant by graft-host diseases, myocardioinfarction, interbowel diseases or osteoarthritus. Diabetes includes Type-I diabetes, Type-II diabetes, diabetes insipidus, gestational diabetes, neurogenic diabetes, nephrogenic diabetes and dipsogenic diabetes. Each of these diseases requires different treatment.

Response to the Remarks of 01-15-2009

Applicants cite US v. Telectronics, 8 USPQ2d 1217 (Fed. Cir. 1988) supposedly in support of the premise that the test for enablement is whether one skilled in the art canuse the invention without undue experimentation from the patent specification disclosue and dinformation known in the art at the time the patent application was filed. US v. Telectronics states "To be enabling under section 112, the patent must contain a description sufficient to enable one skilled in the art to … use the claimed invention." One skilled in the art is not taught how to use the invention, at least to the extent of treating cancer, diabetes, graft-host diseases, mycardioinfarction [sic], interbowel diseases or osteo arthritus [sic], because such a person would not know what such diseases are. In addition, Wikipedia, Sirolimus (already of record) confirms the inability of Rapamycin, a p70S6J inhibitor, to control all cancers on it own. Sawyers, Nature Reviews - Cancer (already of record) confirms that Rapamycin is not effective in all renal cancer patients.

Applicants cite Northern Telecom, Inc. v. Datapoint Corp., 15 USPQ2d 1321 (Fed. Cir. 1990) in support of the proposition that determination of enablement is based on whether a person skilled in the pertinent could use the invention without undue experimentation. As noted above, one skilled in the art is not taught how to use the invention, at least to the extent of treating cancer, diabetes, graft-host diseases, mycardioinfarction [sic], interbowel diseases or osteo arthritus [sic], because such a person would not know what such diseases are. The teachings of Wikipedia and Sawyers have been considered above.

Applicants cite Fields v. Conover, 170 USPQ 276, 279 (CCPA 1971) to support the premise that undue experimentation requires a level of ingenuity beyond what would be expected of one of ordinary skill in the art. However, Fields v. Conover concerned a "how to make" situation, not a "how to use" situation as in the present case.

In re Certain limited-Charge Cell Culture Microcarriers, 221 USPQ 1165, 1174 stated "Thus, the fact that experimentation may be complex, as testified to in this case, does not necessarily make it undue, if the art typically engages in such experimentation." Here, the experimentation is undue because, as noted above, one of ordinary skill in the art would not recognize many of the diseases or conditions said to be treated by the present claims and because Wikipedia and Sawyers question to ability of another p70S6J inhibitor, Rapamycin, to control all conditions in all patients.

All of the factors listed in In re Wands, 8 USPQ2d 1400, 1404 to determine undue experimentation have been considered in detail above.

This rejection under 35 USC 112, paragraph 1, is not based on a requirement for the applicant to disclose a test with each species covered by a claim. In re Angstadt, 190 USPQ 214 (CCPA 1976). The rejection is made because a person of skill in this art would not recognize certain diseases recited in the claim, and because the prior art presents valid reasons to question the ability of the present method to treat all cancers in all patients.

The references cited by Applicant to Peralba, Pene, Miyakawa and Le were each considered in detail in the Final Rejection and that discussion is incorporated here in its entirety. Applicants newly cite articles by Um, et al., Nature 431, 200-205, 2004 and Pende, et al. Nature 408, 994-997, 2000. If Applicants wish these articles to be considered on the record, they must provide copies thereof for the examiner's consideration.

Applicants also cite BMC Cardiovascular Disorders 2004, 4:6 for its discussion of the implication of p70S6K in angiotensen II induced protein synthesis in rat aortic vascular smooth muscle cell and cardian myocyes. If Applicants wish to establish how this information relates to the treatment of the diseases and conditions recited in the claim, the examiner will be happy to consider such information.

Applicants avoid any discussion of Sitrick v. Dreamworks LLC, 85 USPQ2d 1826, 1830 (Fed. Cir. 2008) and Automotive Tech. Int'l. v. BMW of N. America, Inc., 84 USPQ2d 1108, 1116 (Fed. Cir. 2007. These two cases appear to be the most pertinet to the present fact situation and support the examiner's position.

Accordingly, claim 40 will not be entered because it would be rejectable under 35 USC 112, paragraphs 1 and 2. Cancellation of claim 40 will result in the allowance of this application.